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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,818	01/26/2004	Patricia A. Brown	108328.00170 (AVSI-0033)	8276

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,818	BROWN ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2007*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9,11,15-19,22,23,26-28,30,34-38,40-45,47,48 and 52-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-4,7-9,11-19,22,23,26-28,30-38,40-45,47-57,63,69,75,77,79,80,86,89,97 and 99.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 12-14, 31-33, 49-51, 63, 69, 75, 77, 79, 80, 86, 89, 97, and 99

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/12/07 has been entered.

An amendment was received and entered on 3/12/07.

Claims 20 and 39 were canceled.

Claims 1-4, 7-9, 11-19, 22, 23, 26-28, 30-38, 40-45, 47-57, 63, 69, 75, 77, 79, 80, 86, 89, 97, and 99 remain pending in the instant application.

Claims 12-14, 31-33, 49-51, 63, 69, 75, 77, 79, 80, 86, 89, 97, and 99 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/15/06.

Claims 1-4, 7-9, 11, 15-19, 22, 23, 26-28, 30, 34-38, 40-45, 47, 48, and 52-57 are under consideration in this Office Action.

Rejections Withdrawn

Rejections not reiterated from the previous action are withdrawn.

Claim Objections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Written Description

Response to Arguments

Applicant's arguments filed 11/6/06 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37, 38, 40-45, 47, 48, and 55-57 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al (WO

200261037 A2) in view of Aihara et al (Nature Biotech. 16: 867-870, 1998) and Simon (US 6,928,318).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Schwartz taught injection of pSPc5-12-HV-GHRH (SEQ ID NO:11) into the muscle of a farm animal, and subsequent electroporation at the site by the method of Aihara. Pigs are exemplified at the paragraph bridging pages 37 and 38. Other animals include dairy cows, see paragraph 23. Aihara taught a method of electroporating nucleic acids into muscle by inserting electrode needles into muscle such that they encompassed the site into which DNA is injected. See page 867, column 2, second full

paragraph. So, it is clear that the method of Schwartz includes delivery of nucleic acid to an area of tissue that is surrounded by and penetrated with a plurality of needles.

Schwartz did not teach application of a constant current electrical pulse.

Simon taught an electroporation system for introducing nucleic acids into muscle that utilizes a constant-current pulse generator where the delivered current is constant and substantially independent of a change in a resistance in the selected tissue. See specifically column 12 lines 17-51, and column 18, lines 55-58.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the electroporation of Simon because it allows such advantages as enabling accurate measurement and recording of the entire time course of relevant electrical parameters during electroporation. This facilitates optimization of conditions. See column 18, lines 14-22.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent. With regard to limitations requiring a reduction in mortality of newborns (claims 3 and 4) note that Schwartz envisioned methods of delivery to pregnant farm animals. See paragraphs 15-22 at pages 6-12.

Regarding limitations concerning the mass of nucleic acid construct given, these limitations are obvious because the mass given is a result effective variable. See paragraph 140 on page 40 of Schwarz.

Claims 15-17, 34-36, and 52-54 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz et al (WO 200261037 A2), Aihara et al (Nature Biotech. 16: 867-870, 1998) and Simon (US 6,928,318), as applied to claims 1-4, 7-9, 11, 18-19, 22, 23, 26-28, 30, 37, 38, 40-45, 47, 48, and 55-57 above, and further in view of Fewell et al (US 2003/0109478).

The teachings of Schwartz, Aihara, and Simon are discussed above and render obvious methods of delivering to a farm animal SEQ ID NO:11 by injection into muscle and subsequent electroporation by positioning multiple needle electrodes around the injections site and delivering a constant current pulse.

These references do not teach use of a transfection-facilitating polypeptide.

Fewell taught a method of improving delivery of a nucleic acid expression construct to muscle cells in vivo comprising introducing into the muscle a nucleic acid expression construct and poly-L-glutamate, and electroporating the muscle tissue using needle electrodes. See entire document, e.g. first sentence of paragraph 109 at page 11, paragraphs 113 and 114, paragraph 123 bridging pages 12 and 13, paragraph 128 at page 13, and claim 79.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the poly-L-glutamate of Fewell in the method of Schwartz as modified above in order to obtain the reasonably expected improvement in delivery and expression.

Response to Arguments

Applicant's arguments filed 3/12/07 have been fully considered but they are not persuasive.

Applicant addresses the obviousness rejections at pages 17-21 of the response. Essentially, Applicant argues that Simon does not teach maintaining a constant current pulse under a threshold to enable the user to reduce cell heating and create less cell death. Applicant states that Simon's device records electrical parameters concurrently with biological responses only to correlate them and assess the performance of the system, relying for support on Simon at column 5, line 59 to column 6, line 11. Applicant concludes that Simon provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is unpersuasive. Applicant's attention is directed to Simon at column 12, lines 33-49. This passage indicates that the electroporation apparatus includes a signal amplifier comprising a gain adjustable operational amplifier with a feedback arrangement that can be configured to control for constant current ("CC") or constant voltage ("CV") feedback. This passage also indicates that the electrical characteristics of a tissue being treated "may vary somewhat in time (generally, the resistance of tissue is observed to fall during treatment). In operation as a constant current amplifier, signal generator 10 decreases the voltage output level if the average current increases above a predetermined value." Therefore, the apparatus of Simon does maintain a constant current below a threshold. This would clearly allow a user to reduce cell heating and create less cell death. For these reasons the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 7-9, 11, 18, 19, 22, 23, 26-28, 30, 37, 38, 40-45, 47, 48, and 55-57 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-23 of U.S. Patent No. 6,423,693, in view of Schwartz et al (US Patent 6,551,996) and Simon (US 6,928,318).

Claims 21-23 of '693 are drawn to methods of delivering to muscle cells in vivo an expression vector encoding GHRH, wherein the vector comprises 5' and 3' UTRs. The portion of the specification supporting the claims indicates that method is intended for livestock improvement. See column 3, lines 8 and 9, and column 35, lines 20-41.

The '693 patent does not claim a synthetic muscle specific promoter or constant current electroporation.

The '996 patent taught a method of injecting into muscle of a farm animal a plasmid vector encoding SEQ ID NO:1 (HV-GHRH, an optimized protease resistant form of GHRH) under the control of a synthetic muscle specific promoter (SPc5-12). The site of injection was subsequently subjected to electroporation. See column 6, lines 15-24, column 22, lines 10-30. The method is intended to improve growth performance and increase the efficiency of the animal. See abstract, column 8, lines 24-60, and column 17, lines 31-34.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the promoter of '996 in the method of '693. One would have been motivated to do so because '996 taught that the SPc5-12 promoter greatly exceeds the transcriptional potencies of natural muscle specific promoters. See column 3, lines 45-50.

Simon taught an electroporation system for introducing nucleic acids into muscle that utilizes a constant-current pulse generator where the delivered current is constant and substantially independent of a change in a resistance in the selected tissue. See specifically column 12 lines 17-51, and column 18, lines 55-58.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the electroporation of Simon because it allows such advantages as enabling accurate measurement and recording of the entire time course of relevant

electrical parameters during electroporation. This facilitates optimization of conditions. See column 18, lines 14-22.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent.

Claims 15-17, 34-36, and 52-54 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 21-23 of U.S. Patent No. 6,423,693, Schwartz et al (US Patent 6,551,996), and Simon (US 6,928,318) as applied to claims 1-4, 7-9, 11, 18, 19, 22, 23, 26-28, 30, 37, 38, 40-45, 47, 48, and 55-57 above, and further in view of Fewell et al (US 2003/0109478).

The teachings of the '693 and '96 patents are discussed above. These references did not teach a transfection facilitating polypeptide.

Fewell taught a method of improving delivery of a nucleic acid expression construct to muscle cells in vivo comprising introducing into the muscle a nucleic acid expression construct and poly-L-glutamate, and electroporating the muscle tissue using needle electrodes. See entire document, e.g. first sentence of paragraph 109 at page 11, paragraphs 113 and 114, paragraph 123 bridging pages 12 and 13, paragraph 128 at page 13, and claim 79.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the poly-L-glutamate of Fewell in the method of '693 in order to obtain the reasonably expected improvement in delivery and expression.

Although the cited references are silent with respect to an involuntary cull and body condition score, the combined references render obvious all of the claimed active method steps, so the functional effects of the methods are considered to be inherent.

Response to Arguments

Applicant's arguments filed 3/12/07 have been fully considered but they are not persuasive.

Applicant addresses the rejections at pages 19-21 of the response, reiterating the arguments set forth above against the Simon reference, i.e. Simon provides no teaching of maintaining the actual constant current electrical pulse below a threshold. This is unpersuasive for the reasons set forth above, i.e. the apparatus of Simon does maintain a constant current below a threshold by means of a feedback arrangement. Simon specifically mentions the fact that resistance in a cellular sample can decrease with time, and so in constant current mode the apparatus will decrease voltage if current rises above a preset threshold. This results in a decrease in current to the threshold. For these reasons the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the

hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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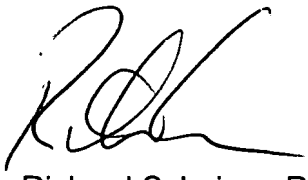

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